REMARKS

Claims 7, 9, 10, and 18 to 20 are now pending in this application. Claim 7 has been amended to recite the terms "one or more" and "exoantigen," and claims 8 and 15 have been canceled without prejudice. Claim 18 has been amended to depend from claim 7 and to replace the phrase "is capable of binding" with "binds to." New claim 20 has been added. Support for the amendment to claim 7 exists in the specification, for example, at page 1, line 31 to page 2, line 1; for amended claim 18 and new claim 20, for example, at page 16, lines 3-7. The amendments add no new matter to the application.

Withdrawn Rejections

Applicants acknowledge the Office's withdrawal of the following rejections:

(a) the rejection of claims 7 to 9 under 35 U.S.C. §102(b);

(b) the rejection of claims 7 to 10 under 35 U.S.C. §103(a); and

(c) the rejection of claim 18 under 35 U.S.C. §103(a).

35 U.S.C. § 102

Claim 15 has been rejected as allegedly anticipated by Stuart et al., *Immunology* **68**:469-473 (1989). Applicants respectfully disagree that Stuart anticipates claim 15. However, in the interest of moving the present application toward allowance, applicants have canceled claim 15 without prejudice, thereby obviating this rejection.

35 U.S.C. § 103: Claims 7 to 9 and 18 to 19

Claims 7 to 9, 18, and 19 have been rejected as allegedly obvious over Whittum-Hudson et al. (*Nature Medicine* **2**:1116-1121 (1996)) in view of Dick, Jr. et al. (*Conjugate Vaccine, Contrib. Microbiol. Immunol.* **10**:48-114 (1989)).

Applicants respectfully disagree and submit that amended claim 7 (and all claims that depend from claim 7) are not rendered obvious over Whittum-Hudson in view of Dick, Jr. Amended claim 7 recites a composition comprising a carrier group covalently coupled to an

isolated chlamydial glycolipid exoantigen (GLXA) oligosaccharide. On the other hand, Whittum-Hudson describes the production of GLXA anti-idiotypic antibodies and their use as a vaccine to protect against *C. trachomatis* infections. Whole GLXA was used to produce such antibodies (see, e.g., Whittum-Hudson at page 117, second column). Whittum-Hudson does not describe, or even suggest, an isolated GLXA *oligosaccharide* covalently coupled to a carrier group. Nowhere does Whittum-Hudson disclose or suggest that useful oligosaccharides should, or even could, be isolated from GLXA and coupled to a carrier group.

The Office Action also cites Dick, Jr. However, this reference does not provide the information missing from Whittum-Hudson. Dick, Jr. describes how to make certain glycoconjugate vaccines; i.e., vaccines based on capsular polysaccharide immunogens (CPS) and lipopolysaccharides (LPS). Dick, Jr. does not describe GLXA and, like Whittum-Hudson, it fails to describe, or even suggest, that useful oligosaccharides could be cleaved from (or chemically synthesized based upon) GLXA oligosaccharides, much less that such oligosaccharides could be covalently coupled to a carrier group.

Applicants submit that a skilled practitioner would not have been motivated by Dick, Jr. to modify the methods described in Whittum-Hudson to create the compositions recited in the pending claims. Neither publication describes isolated GLXA oligosaccharides, or suggests that such oligosaccharides are useful and should have been isolated from (or chemically synthesized based on) GLXA, or that they could have been coupled to carriers using the methods taught in the present application. In fact, Whittum-Hudson itself teaches away from making such compositions, as discussed below.

Whittum-Hudson suggests using anti-idiotypic antibodies to make a vaccine against chlamydial infection. Importantly, Whittum-Hudson demonstrates (on page 1118) that when mice were immunized with either a soluble anti-idiotype antibody (mAb_2) or with GLXA, only the mAb_2 was protective against subsequent chlamydial challenge: "Significant reductions in infectious yields were observed [after immunization with mAb_2] even after a >2 log higher challenge dosage, whereas *GLXA in alumina was not protective*" (emphasis added). Given that Whittum-Hudson teaches that whole GLXA itself is not protective, no skilled practitioner would

have been motivated to isolate (or synthesize) an oligosaccharide from GLXA and couple it to a carrier group, nor would he have had any reasonable expectation of success in doing so. Whittum-Hudson would have discouraged skilled practitioners from using GLXA oligosaccharides to make vaccines by stating that such a technique is difficult, that GLXA itself is not protective, and by suggesting that a potentially superior alternative exists, i.e., the use of anti-idiotypic antibodies as vaccines.

Nevertheless, in concluding its argument for finding a case for *prima facie* obviousness, the Office Action states (at page 8-9):

> It would be *prima facie* obvious at the time the invention was made to use [sic] covalently couple the oligosaccharide/polysaccharide of chlamydial GLXA as taught by Whittum-Hudson et al to a carrier protein (e.g. diphtheria toxoid or tetanus toxoid) as taught by Dick, Jr. et al because Whittum-Hudson et al teach that GLXA is abundant in *Chlamydia* species as well as being antigenic and Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins thereby, demonstrating a thymus dependent (TD) response to carbohydrate components and enhancing the immune response to carbohydrate component.

Applicants respectfully disagree. Nowhere does Whittum-Hudson describe isolated GLXA oligosaccharides. Because Whittum-Hudson does not teach isolated GLXA oligosaccharides and does teach that GLXA is not protective, no skilled practitioner would have been motivated to combine the disclosures of Whittum-Hudson and Dick, Jr. in an attempt to arrive at the present invention. Applicants respectfully submit that rather than rendering the presently claimed subject matter obvious, Whittum-Hudson fails to disclose using isolated GLXA oligosaccharides, discourages study of isolated GLXA oligosaccharides for use as vaccines, and encourages the use of anti-idiotypic antibodies as an alternative vaccine.

Therefore, neither of the cited references, alone or in combination, provide a teaching or a motivation for a skilled artisan to arrive at the present claims, nor a reasonable expectation of success in doing so. Applicants respectfully submit that the Office has failed to make a *prima facie* case of obviousness under 35 U.S.C. §103, and request reconsideration and withdrawal of the present rejection.

35 U.S.C. § 103: Claim 10

Claim 10 was rejected as allegedly obvious over Whittum-Hudson and Dick, Jr. in view of Semprevivo (*Carbohydrate Research* **177**:222-227 (1988)). Applicants respectfully disagree for the reasons discussed below.

Claim 10 recites that the linker is 2-(4-aminophenyl)ethylamine and ultimately depends from claim 7 and is thus patentable for at least the reasons discussed above.

Furthermore, Semprevivo does not make up for the deficiencies of Whittum-Hudson and Dick, Jr., but instead describes a method for derivatizing oligosaccharides from the eukaryotic organism *Leishmania mexicana amazonensis*. Semprevivo indicates that similar methods have been utilized for other eukaryotic organisms, such as *Leishmania tropica*, *Leishmania donovani*, *Trichomonas vaginalis*, *Schistosoma mansoni*, and *Nematospiroides dubius*. However, Semprevivo does not describe any chlamydial glycolipids, much less isolated GLXA oligosaccharides. Further, Semprevivo does not disclose, or even suggest, that Semprevivo's methods could have been utilized with glycolipids from prokaryotes of the genus *Chlamydia*, or for that matter, any other prokaryotic organism. Given Semprevivo's lack of instruction on these issues, a skilled practitioner could not have reasonably expected to be successful in using Semprevivo's methods with GLXA oligosaccharides. Thus, none of these three references, singly or in combination, describe or suggest the claimed invention, nor would they have motivated a skilled practitioner to prepare the compositions of the present application with any reasonable expectation of success. Accordingly, applicants respectfully request that this rejection be reconsidered and withdrawn.

Claim 10 was also rejected as allegedly obvious over Whittum-Hudson and Dick, Jr. in view of Smith (*J. Biol. Chem.* **255**:55-59 (1980)). Again, applicants respectfully disagree for the reasons discussed below.

The shortcomings of Whittum-Hudson and Dick, Jr. are discussed above. Smith does not make up for the deficiencies of these two references. Smith describes a method for derivatizing free oligosaccharides from human milk for coupling to proteins and the use of such

oligosaccharide-protein conjugates to generate immune responses in rabbits. Smith does not disclose chlamydial glycolipids, much less GLXA, or the preparation of oligosaccharides from the glycolipid. Further, Smith does not suggest that its methods could have been utilized with an isolated glycolipid oligosaccharide from prokaryotes of the genus *Chlamydia*, or for that matter, any other prokaryotic organism. Thus, the three references would not have motivated a skilled practitioner to prepare the compositions of the present application with any reasonable expectation of success. Applicants respectfully request that this rejection be reconsidered and withdrawn.

It appears that the Office Action relies on the present application to provide a roadmap to show how to combine the cited references. However, to support a proper *prima facie* case of obviousness, the prior art, not applicants' application, must contain the requisite motivation to combine all the cited references. Any other analysis of the art is hindsight, which the courts have long prohibited. For example, in its analysis of whether or not the idea of using a particular cloning method was obvious, the Federal Circuit in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 1209 (Fed. Cir. 1991) found that:

> [T]he realization of that idea [to use a particular cloning strategy] would not have been obvious. There were many pitfalls. *Hindsight is not a justifiable basis on which to find that ultimate achievement of a long sought and difficult scientific goal was obvious* (emphasis added).

The prior art must suggest the combination of the prior art teachings and that such a combination would have a reasonable likelihood of success. That it may be "obvious to try" such a combination is not the proper standard in an obviousness analysis. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987) (an invitation to try an experiment is not the proper test for obviousness); *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529 (Fed. Cir. 1988):

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art ... (Citations omitted) Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure.

Applicants submit that none of the publications cited in the Office Action, singly or in combination, suggest developing the compositions of the present invention. Thus, applicants respectfully request that all of the rejections be reconsidered and withdrawn.

35 U.S.C. § 112, Second Paragraph

The Examiner alleges that claim 18 is indefinite by its use of the term "capable of." Applicants do not agree that the claim is indefinite. However, in the interest of moving the present application toward allowance, applicants have amended claim 18 to recite that the oligosaccharide binds to anti-GLXA monoclonal antibody 89MS30. Accordingly, applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

Applicants respectfully request that the rejections to the claims be withdrawn and that all claims be allowed. Enclosed is a $225 check for the Petition for Extension of Time fee for a two-month extension. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 08952-008001.

Respectfully submitted,

Date: 1/11/05

Reg. No. 54,112

J. Peter Fasse
Reg. No. 32,983

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906
21008749.doc